



### INVITED REVIEW

#### The origin of SARS-CoV-2, history, present and future status of coronaviruses

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#### SARS-CoV-2 orijini, coronavirusların tarihi, bugünü ve gelecek durumu

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#### Öz

Coronavirüsler (CoVs), 2002 yılına kadar insanlarda genellikle soğuk algınlığı ve bazen de zatürre semptomlarına neden olmuşlardır. Ancak 2002 yılından sonra Şiddetli Akut Solunum Yolu Sendromu (SARS) ve Orta Doğu Solunum Yolu Sendromu (MERS) gibi yüksek mortaliteli enfeksiyonlar ile ilişkili yüksek virülenli CoV'ler ortaya çıkmaya başlamıştır ve son olarak Aralık 2019'da ise Çin'de zatürre semptomları ile karakterize yeni bir hastalığın (COVID-19) ortaya çıkmasına sebep olmuşlardır. COVID-19, kısa sürede yayılarak tüm dünyayı etkilemiş ve tüm dikkatleri üzerine çekmiştir. Salgının kontrol altına alınması amacıyla sıkı karantina önlemlerinin yanı sıra kişisel hijyen ve sosyal mesafenin korunması ve kişisel koruyucu ekipman kullanımı ana kural olarak benimsenmiştir. Ayrıca hızlı test kitleri, aşı ve antiviral ilaç çalışmaları hız kazanmıştır. COVID-19 pandemisinin ne zaman biteceği belirsizliğini korumakla beraber, pandemiden elde edilen kazanımlar bir bütün olarak düşünüldüğünde; kazanılan deneyimlerin hastalığın insidansını azalttığı ve belki de pandeminin sona ermesine yardımcı olacağı ve gelecekte olası hafif veya ciddi salgınların kontrolü üzerinde büyük bir etkiye sahip olacağı açıktır. Ayrıca, hayvan orijinli CoV'ların tekrarlayan periyotlarla insanlarda ortaya çıkması ve büyük salgınlara yol açması, veteriner ve beşeri hekimliğin birlikte hareket etmesi bağlamında TEK SAĞLIK konseptinin önemini bir kez daha ortaya koymuştur. Bu derlemenin amacı, tüm dünyanın artık farkında olduğu koronavirüslerin kökeni ve tarihini aktarmanın yanı sıra, CoV'ların mevcut durumunu aydınlatmak ve bir sonraki olası CoVs salgını veya pandemisine hazır olmak amacıyla, CoV'ların gelecekteki olası etkilerini değerlendirmektir.

**Anahtar kelimeler:** Coronavirüsler, COVID-19, HCoVs, pandemi, SARS-CoV-2

#### Abstract

Coronaviruses (CoVs) have generally progressed with common cold and sometimes pneumonia in humans until 2002. However, highly virulent CoVs associated with high mortality infections such as Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome have began to emerge after 2002 and finally caused the emergence of a new disease (COVID-19) characterized by pneumonia symptoms in China in December 2019. COVID-19, transmitted in a short time, has affected to whole world and attracted all the attention. Besides strict quarantine measures, personal hygiene, protection of social distancing and use of personal protective equipment have been adopted as the main rule. Also, rapid test kits, vaccine and antiviral drug studies have accelerated fully. Although it remains uncertain when COVID-19 pandemic will end, when gains from the pandemic are considered as a whole; it is clear that experiences gained from pandemic reduce the incidence and perhaps would help to end of the pandemic and will have a great effect on the control of possible mild or serious epidemics in the future. In addition, emergence of animal origin CoVs causing repetitive epidemics or pandemics in humans has once again demonstrated the importance of the ONE HEALTH concept in collaboration between veterinary and human medicine. The purpose of this review is to convey the origin and history of coronaviruses, which the whole world is now aware of, as well as to enlighten current status of CoVs and evaluate the possible future effects of CoVs in order to be ready for next possible epidemic of CoVs.

**Keywords:** Coronaviruses, COVID-19, HCoVs, pandemi, SARS-CoV-2





## Introduction

Coronaviruses (CoVs) are enveloped RNA viruses that cause acute or persistent infections with a broad host spectrum including humans, other mammals, birds and some wild animals (Knipe and Howley 2013). CoVs belong to *Orthocoronavirinae* subfamily in the *Coronaviridae* family within the *Nidovirales* order (Knipe and Howley 2013). Four genera were classified in the Coronaviridae family including *alpha-*, *beta-*, *gamma-* and *deltacoronavirus* (Cui et al 2019). Seven coronavirus species are known to cause infections in humans. Among these, HCoV-229E and HCoV-NL63 are in *alphacoronavirus*, while HCoV-OC43 and HCoV-HKU1 are included in the *betacoronavirus* genus and usually cause the common cold. SARS-CoV, MERS-CoV and SARS-CoV-2, which cause serious respiratory diseases in humans, are also included in the *betacoronavirus* genus (Knipe and Howley 2013, Cui et al 2019, Wu et al 2020).

Important CoV infections in domestic animals are *Porcine Epidemic Diarrhea Virus* (PEDV), *Severe Acute Diarrhea Syndrome-coronavirus* (SADS-CoV), *Transmissible Gastroenteritis Virus* (TGEV) and *Porcine Respiratory Coronavirus* (PRCoV) in pigs; *Feline Coronavirus* (FCoV) in cats and *Canine Coronavirus* (CCoV) in dogs which belong to the *alphacoronavirus* genus (Decora and Lorusso 2020). *Bovine Coronavirus* (BCoV), *Equine Coronavirus* (ECoV), and *Porcine Hemagglutinating Encephalomyelitis Virus* (PHEV) infecting cattle, horses and pigs, respectively, are included in the *betacoronavirus* genus. Gammacoronaviruses generally infect avian species. Deltacoronaviruses have an infection potential in pigs (Knipe and Howley 2013, Decora and Lorusso 2020, Özcan and Tamer 2020).

CoV are enveloped viruses which include a non-segmented, positive polarity and single stranded RNA genome consists of a base number ranging from 26,000 to 37,000, the largest known genome within RNA viruses (Weiss and Navas-Martin 2005, Knipe and Howley 2013). CoV genomic structure is in the form of a 5'-leader-UTR-replicase-S (Spike) -E (Envelope) -M (Membrane) -N (Nucleocapsid) -3'-UTR poly (A) tail. The S protein is responsible for binding to the cell receptor and subsequently the entry of the virus into the host cell. M and E proteins contribute greatly to the formation of new virus particles. N protein is necessary for viral RNA synthesis (Fehr and Perlman 2015, Song et al 2019). CoV have a variety of host ranges in nature and can often cross the host species barrier (Chan et al 2013). Cross-host species interactions are associated with changes and interactions between different regions of the S protein. Most human coronaviruses are reported to originate from bat coronaviruses, either directly or through intermediate host transmission (Hulswit et al 2016).

## Discovery and historical development of coronaviruses

CoVs were first discovered in 1937 as an infectious bronchitis (IBV) agent causing respiratory disease in chickens (Beaudette and Hudson 1937). Later, it was isolated from an infectious gastroenteritis (TGEV) case in pigs in 1946 (Doyle and Hutchings 1946), and as agents of infectious and severe hepatitis and neurological diseases (MHV) of mice in 1949 (Cheever et al 1949). Until the 1960s, although these viruses had similar characteristics, their grouping together with some human respiratory viruses was not accepted (Knipe and Howley 2013). The first human coronavirus (HCoV) was isolated in 1965 from the respiratory tract of a person suffering from the common cold and was named B814 (Tyrrell and Bynoe 1966). During the same period, other researchers isolated same virus from samples collected from medical students with the common cold and named it as 229E (Hamre and Procknow 1966). McIntosh et al (1967) revealed that mixed strains isolated from the human respiratory system were ether-sensitive infectious agents and were named as "OC" because they could be produced in organ cultures. Following these developments, infected organ cultures with B814 were examined under electron microscope and it was reported that they were particles resembling infectious bronchitis virus 80-150 nm in size (Almeida and Tyrrell 1967). In the late 1960s, different human and animal virus strains including MHV, IBV and TGEV were examined under electron microscopy and this family of viruses was named CORONA, because of the crown-like formations on the virion surface structure of the viruses (McIntosh et al 1967, Witte et al 1968, Tyrrell et al 1975). The most important common features detected under electron microscopy were a pointed fringe that derives from the virion surface, thickens towards the tip and is called a large surface spike. Due to this characteristic spike in the shape of a halo, this new virus group was named the solar crown (corona) (Knipe and Howley 2013). Examining the epidemiological characteristics of human coronavirus, it has been determined that they are seen more in winter and spring seasons with rainfall than in summer and are more related to various respiratory diseases (McIntosh et al 1970, Jahangir et al 2020). The predominant disease is associated with pneumonia in children and young adults; chronic bronchitis and asthma in adults and elderly (Jahangir et al 2020). It was thought that two coronaviruses (229E and OC) were responsible for a significant part of the common cold in humans, especially in the winter months. This pre-conception changed dramatically in 2002 with the emergence of severe acute respiratory syndrome (SARS), a new disease caused by SARS-CoV; an unknown coronavirus (Drosten et al 2003, Ksiazek et al 2003, Peiris et al 2003). However, after the SARS epidemic, two more common human respiratory coronaviruses (HCoV-NL63 and HCoV-HKU1) were discovered with studies conducted until 2005 (Van Der Hoek et al 2004, Woo et al 2005).



Another coronavirus outbreak was seen in Saudi Arabia with a higher case fatality rate in 2012, but the number of cases were not very high due to its low morbidity (Han et al 2020, WHO 2020h). In late 2019, COVID-19 caused by SARS-CoV-2 emerged with an uncertain duration and it was declared as a global pandemic.

CoVs were first identified in animals in 1937 and in humans in the 1960s. However, how long they have been existing is unknown. They have often been associated with mild illness, but when evaluated over the past two decades, a highly virulent strain emerges every few years. (Bexaudett and Hudson 1937, Tyrrell and Bynoe 1966, Yang et al 2020).

### The current status of human coronavirus

Pathogenesis of HCoV infections, especially SARS-CoV-2, is still not fully illuminated. Even before 2019; there were six known CoVs that cause respiratory disease in humans. HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1 are occasionally referred to as the "common cold" and cause generally mild symptoms, but they can sometimes cause severe infections in infants, children and older people. Human CoVs (HCoVs) are associated with almost 15-29 % of common cold cases, while SARS-CoV-2 is a zoonose with symptoms ranging from lighter flu-like symptoms to more severe symptoms that might end in death (Isaacs et al 1983, Fehr and Perlman 2015, Su et al 2016, Yang et al 2020). Seven HCoVs and their characteristics are summarized in Table 1.

### The SARS epidemic

Atypical pneumonia caused by SARS-CoV was first seen in Foshan city in Guangdong province in Southern China in November 2002. Severe acute respiratory symptoms appeared in a man in Guangzhou city who had close contact with

wild animals and their feed, working in a restaurant as chef in December 2002. The virus spread rapidly globally with person-to-person transmission within three months (Zhong et al 2003).

A professor of medicine from Foshan city, travelled to Hong Kong to visit his relations on February 21, 2003, infected a total of 16 people (Yang et al 2020). SARS-CoV spread to 29 countries, including Hong Kong, Vietnam, Singapore and Canada, resulting with 8096 infected case and 774 deaths. The SARS case fatality rate was recorded as 9.6%. It was notified that the last SARS outbreak was extinguished on May 18, 2004. No confirmed case except suspicious cases has not been reported after that date (WHO 2020a).

Initial stages of outbreaks in Hong Kong, China and other countries, nobody had a detailed information about the deadly SARS-CoV. Even samples were not collected for virological studies during the first cases, so virus isolation was only possible in February when the epidemic curve began to increase and the genome of SARS-CoV was sequenced in about 3 months (Zhong et al 2003). Both phylogenetic studies and serological studies showed that the origin was horseshoe bats (*Rhinolophus sinicus*) (Li et al 2005). The intermediate hosts have been proven to be civet cats (*Paguma larvata*), raccoon dogs (*Nyctereutes procyonoides*) and also Chinese ferret badgers (*Melogale moschata*) who could be infected experimentally (Wang and Eaton 2007). The basic reproduction number (R<sub>0</sub>) was calculated to be between 2.7-3.4 (Chen et al 2020, Han et al 2020). Global success in combating SARS was partly due to the epidemiology and properties of the virus. The determination of the transmission routes of the virus, diagnosis and confirmation of the infected patients led to successfully implemented isolation measures and helped greatly reduce the transmission of the disease (Anderson et al 2004). On the other hand, more than 62,000 healthcare professionals were trained in the SARS patient handling practices, and the uti-

Table 1. Human Coronaviruses features

Virus Name	Genus	Symptoms	Mortality (%)	Notification of detection
HCoV-229E	<i>Alphacoronavirus</i>	Upper respiratory, mild disease (Usually)	N/A	1966-continue
HCoV-NL63	<i>Alphacoronavirus</i>	Upper respiratory, mild disease (Usually) Bronchiolitis or pneumonia (Rarely)	N/A	2004-continue
HCoV-OC43	<i>Betacoronavirus</i>	Upper respiratory, mild disease (Usually)	N/A	1967-continue
HCoV-HKU1	<i>Betacoronavirus</i>	Upper respiratory, mild disease (Usually) Bronchiolitis or pneumonia (Rarely)	N/A	2005-continue
SARS-CoV-1	<i>Betacoronavirus</i>	Severe acute respiratory syndrome	9,6	2002-2003
MERS-CoV	<i>Betacoronavirus</i>	Severe acute respiratory syndrome	35,7	2012-continue
SARS-CoV-2	<i>Betacoronavirus</i>	Severe acute respiratory syndrome	2,82	2019-continue





lizing PPE during the SARS epidemic (Pang et al 2003). Although SARS spread globally at high speed and caused great damage to public health, ultimately the worldwide success in containing SARS has shown the possibility of disease containment (Christian et al 2004). Many regulations on the prohibition of wild animals came into force after SARS epidemic in China, but these could not prevent illegal trade (Zhong and Zeng 2008, Yang et al 2020).

### The MERS epidemic

A new coronavirus different from the previous ones was isolated from a man who died from severe pneumonia and kidney failure in Saudi Arabia in 2012 (Zaki et al 2012). This novel disease was called Middle East Respiratory Syndrome (MERS) and the agent was identified as MERS-CoV. Phylogenetic analysis of other betacoronaviruses isolated from bats with MERS-CoV showed that they are very close and MERS-CoV and bat coronaviruses such as BtCoV-HKU4 and BtCoVHKU5 were found in same lineage (Boheemena et al 2012). Serological and virological studies were carried out on cattle, sheep, goats and different camel species in order to investigate the epidemiologic relation of MERS. MERS-CoV antibody was identified in dromedary camels serologically showing that it could be intermediate host (Reusken et al 2013). According to the latest data of FAO, the disease has been detected in 2527 people in 27 different countries and 904 deaths occurred by February 2020, with a case-fatality rate of 35.7% (Fig.2) (FAO 2020). MERS-CoV mortality was 3.6 times higher than SARS-CoV, while the R0 value was moderately low (0.8-1.3), resulting in a slow spread among human populations (Chen et al 2020).

### The COVID-19 pandemic

Unknown disease with severe acute pneumonia symptoms first appeared on 12 December 2019 in Wuhan city, Hubei province of China. The number of cases increased in a short time due to human-to-human transmission became an epidemic in the city (Zhou et al 2020). The infection, later named as COVID-19, started to spread all over the world in January 2020. It has spread to more than 200 countries as of October 2020 (WHO 2020b). World Health Organization (WHO) declared COVID-19 as a global pandemic in March 2020 (Di Gennaro et al 2020). Studies on the disease and its agent continue at full steam. Revealing the etiology, pathogenesis and epidemiology of COVID-19 completely will help to more proactively about the future of the disease, as well as vaccine and drug studies.

### The origin of SARS-CoV-2

Officially, the first notification related to the disease was made by the Wuhan Municipal Health Commission that on 31 December 2019 and research on the cases was ongoing

(WHO 2020e). After much speculation about the disease, the Chinese Center for Disease Control and Prevention (CDC) announced the definition of a new CoV on 9 January 2020 (Gralinski and Menachery 2020). Laboratory studies were also on their way to establish the cause after ruling out the most common pathogens related to respiratory diseases, such as influenza, adenovirus, and mycoplasma. PanCoV molecular tests of bronchoalveolar lavage swabs from patients with worsening pneumonia symptoms found that it is a coronavirus. The whole genome was then sequenced (Zhou et al 2020) and uploaded to GenBank and the GISAID. On 12 January 2020, the gene sequences were made available to researchers all over the world (WHO 2020f). The source of transmission of the new coronavirus 2019 (nCoV-2019) is considered to be the wet-market in Wuhan, Hubei Province, China (Huang et al 2020). The first case reports of the disease revealed that patients originally worked or traded in this market (Wu et al 2020, Zhou et al 2020). It has been reported that various species of live animals, such as bats, frogs, snakes, birds, marmots and rabbits, are sold in the market (Wang et al 2020). During the initial stages of the outbreak, people with symptoms of coronavirus pneumonia were suggested to have visited the Hunan market or consumed as food with infected animals sold there or came into contact with them. However, the presence of infection in those who have not come into contact with these animals suggests human-human transmission (Li et al 2020).

With the first phylogenetic tree created and the full genome sequence of 29,903 bp obtained by meta-transcriptomic sequencing, SARS-CoV-2's most SARS-like bat coronaviruses were determined to be bat-SL-CoVZC21 and bat-SL-CoVZC45, which have 89.1% sequence homology and are products of the recombination of previously identified bat coronaviruses (Wu et al 2020). In the second molecular study, the 29,891 bp whole genome sequence obtained by metagenomics and next-generation sequencing technology showed 79.6% nucleotide homology with the strain SARS-CoV BJ01. Although its nucleotide similarity with SARS-CoV is low, due to the amino acid (aa) similarity of 94.4%, it is thought to belong to the same or a similar species (SARSr-CoV). A phylogenetic analysis performed on other SARSr-CoVs found that the coronavirus BatCoV RaTG13 obtained from *Rhinolophus affinis* bats in Yunnan Province have 96.2 similarities, indicating that bats could be the origin of SARS-CoV-2, and it was suggested that its closest relative is RaTG13. This new virus was originally named novel coronavirus 2019-nCoV (Zhou et al 2020). It has been reported that SARS-CoV-2 and BatCoV RaTG13 form a separate lineage from other SARS-CoVs, which refutes the idea that SARS-CoV-2 emerged as a result of recombination (Paraskevis et al 2020).

The International Committee on Virus Taxonomy (ICTV) Coronavirus Working Group (CSG) studied *Coronaviridae* family's classification and taxon nomenclature (taxonomy).



After considering the phylogenetic and taxonomic characteristics of the human pathogen, the virus temporarily named 2019-nCoV was officially declared to be closely related to the acute respiratory syndrome-associated coronaviruses (SARS-CoVs) and officially re-named *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) (Gorbalenya et al 2020). The new disease, known as novel coronavirus-2019, was officially named COVID-19 by the WHO on 11 February 2020 (WHO 2020d).

Similar to SARS-CoV, SARS-CoV-2 uses ACE2 to infect host cells. Binding of SARS-CoV-2 S to ACE2 was found to have an affinity roughly 10–20 times higher than SARS-CoV S, which may be why SARS-CoV-2 has a stronger likelihood of human-to-human transmission than SARS-CoV (Wrapp et al 2020, Zhou et al 2020).

CoVs can cross species barriers, and SARS-CoV-2 is thought to originate from wild-life in Wuhan (Yang et al 2020). In studies of whether SARS-CoV-2 had an intermediate host like other highly pathogenic HCoVs, whole genome sequences were used. The similarity of SARS-CoV-2 and BatCoV RaTG13 with the SARS-CoV-like CoV (Pangolin-CoV) isolated from Malayan Pangolin were found to be 91.02% and 90.55%, respectively. After RaTG13, the closest virus to SARS-CoV-2 is Pangolin-CoV. The S1 protein of Pangolin-CoV is closer to SARS-CoV-2 than RaTG13. There are five amino acid residues involved in interacting with human ACE2. These amino acids are highly homologous between Pangolin-CoV and SARS-CoV-2, with four amino acid mutations in RaTG13. Neither Pangolin-CoV nor RaTG13 has a putative furin recognition sequence at the S1/S2 cleavage site observable in SARS-CoV-2 (Zhang et al 2020). In another report, aa similarities in the E, M, N and S genes of the virus between Pangolin-CoV and SARS-CoV-2 were found to be 100%, 98.2%, 96.7% and 90.4%, respectively (Xiao et al 2020). These two studies show that pangolins are natural reservoirs of CoVs-like SARS-CoV-2. Furthermore, in the analysis and comparison of the interactions of the important aa involved in binding the S protein (RBD region) and ACE2, it has been shown that pangolins and snakes, as well as turtles, could be intermediate hosts (Liu et al 2020).

### The current status of COVID-19

The clinical picture and risk components of COVID-19 are highly changeable, with the clinical signs ranging from asymptomatic to severe symptoms and death (Phan 2020). As of 16 October 2020, there are 38,789,204 cases and 1,095,097 deaths worldwide; the case-fatality ratio is 2.82%. The highest number of case confirmations in a single day is 387,617, recorded on 10 October 2020, and the highest number of deaths in a single day is 12,438, recorded on 17 April 2020. When the geographical distribution of the cases is examined, the disease, which was first reported in China, was found in Europe in February 2020 and then spread to other regions of

Table 2. The case-fatality rates of the 20 countries with the highest number of cases

Countries	Cumulative Cases	Cumulative Deaths	Case-Fatality Ratio (%)
United States of America	7.833.851	215.199	2,75
India	7.370.468	112.161	1,52
Brazil	5.140.863	151.747	2,95
Russian Federation	1.369.313	23.723	1,73
Argentina	931.967	24.921	2,67
Colombia	930.159	28.306	3,04
Spain	921.374	33.553	3,64
Peru	856.951	33.512	3,91
Mexico	829.396	84.898	10,24
France	780.994	32.868	4,21
South Africa	698.184	18.309	2,62
The United Kingdom	673.626	43.293	6,43
Iran	517.835	29.605	5,72
Chile	486.496	13.434	2,76
Iraq	416.802	10.086	2,42
Bangladesh	384.559	5.608	1,46
Italy	381.602	36.372	9,53
Indonesia	349.160	12.268	3,51
Philippines	348.698	6.497	1,86
Germany	348.557	9.734	2,79

the world. The disease was declared in the United States (US) at the beginning of March 2020, and the US has the greatest number of cases (7,833,851) and deaths (215,199) as of 16 October 2020 (WHO 2020b).

Total number of confirmed cases and deaths of the 20 countries in which case numbers are highest are given in Table 2.

### Control and mitigation measures

As human-human transmission became evident in the spread of COVID-19, extreme quarantine measures were undertaken. Preventing entry into and exit from large cities, as well as countries closing their borders, isolating people at home, and instituting curfews, began to be implemented in January 2020. However, COVID-19 had already spread from China to other countries by this time (Yang et al 2020). According to the most recent data reported by the WHO, the disease is still not controlled and even shows an increasing trend in some countries (WHO 2020b). In some countries, mitigated control and measures are currently reactivated due to expectations of a second wave of infections.





Following the SARS-CoV-2-induced pneumonia outbreak in China, the level I public health emergency action plan was activated across the country. Thus, the most comprehensive and stringent control mitigation measures for public health were implemented. The virus was rapidly detected and sequencing analysis was carried out (Tan et al 2020). After the virus spread across the world and was declared a pandemic, effective quarantine measures were implemented, travel restrictions were imposed, schools were closed, and in-person social activities were limited; life came to a standstill. In addition to the necessity of using masks as protective equipment, such as masks, in some places, unprecedented vaccination and drug studies have begun. In June 2020, control measures began to be relaxed, but as of October 2020, these measures remain in effect in some countries. Although the number of cases has decreased in some countries, it continues to increase in others.

### Transmission parameters

It is difficult to calculate the approximate infection mortality rate (IFR) and case-fatality rate associated with COVID-19 at this time. Doing so requires the need to the collection of serosurvey results and know the precise case and death rates at the countries level. However, as of 4 August 2020, there are countries with mortality rates between 0.5–1% and case-fatality rates ranging from 0.1% to 25% (WHO 2020c). The case-fatality rates of the 20 countries in which case numbers are highest are given in Table 2.

Since the pandemic progresses with varying incidence and prevalence rates across the world, it is difficult to perform an exact calculation of the  $R_0$  value. It was calculated as 2.43–3.10 in Italy (D'Arienzo and Coniglio 2020), and in India, it was 1.62 during the initial stages of the epidemic and 3.43 in the peak stage (Saurabh et al 2020).  $R_0$  values between 1.2–1.8 were reported in a simulation study that included 19 countries, and the average  $R_0$  value in the American countries was 1.4. These are lower than the 2.2, 2.6, 3.8 and 6.47  $R_0$  values obtained from simulations involving China (Anastassopoulou et al 2020, Li et al 2020, Manrique-Abril et al 2020).

An important factor in the spread of viruses is the asymptomatic individuals. While symptomatic patients are isolated in the home or hospital, depending on their clinical condition, asymptomatic patients pose a risk because they may go undetected without testing and are critical in the spread of the virus. In studies of MERS, it has been reported that the asymptomatic rate in positive MERS-CoV cases is between 0–28.6% (Al-Tawfiq 2020). In addition, 0.06% positivity was determined in a serological study of the presence of MERS-CoV in asymptomatic individuals in Korea (Song et al 2018). During the SARS epidemic in Singapore, it was reported that 13% of SARS-positive cases in healthcare workers were

asymptomatic (Wilder-Smith et al 2005). In the COVID-19 pandemic, all countries are concerned about asymptomatic carriers. For this reason, the WHO (2020g) recommends that even if one feels healthy, it is necessary to wear masks, maintain social distancing, and follow hygiene rules. In Italy, 2.6% and 1.2% positivity rates were detected in two different molecular surveys at the beginning and end of the 14-day quarantine period applied in the region where the disease first appeared; interestingly, 43.2% of positive cases were reportedly asymptomatic (Lavezzo et al 2020).

### Information sharing

In the evaluation, analysis and control of an outbreak, it is important to share information about the disease in a clear and timely manner (Abdullah et al 2003). Technology has been commonly used to share information during the COVID-19 pandemic. Data related to the pandemic are shared via both national and international channels, disease notifications are made in a timely manner, and daily data are shared with the public and the WHO. Technology has allowed areas experiencing an outbreak to be marked at the level of geographical coordinates, helping people to be aware of areas where they should be more careful. Access to all kinds of information is provided via television, computer and mobile phones. Additionally, the scientific community shares all kinds of scientific publications with the community without barriers to access. Since the outbreak in December 2019, thousands of articles have been published and have reached a record level. Conducting so many studies on the COVID-19 pandemic, globally and with the support of many countries, provides hope that SARS-CoV-2 will be controlled and eradicated in the near future.

While many studies and struggles regarding COVID-19 continue, it is clear that in many countries, the scientific research efforts as well as social life have been influenced by the COVID-19 pandemic (Naguib et al 2020, Yang et al 2020).

### The future of coronaviruses

SARS-CoV, MERS-CoV and SARS-CoV-2 outbreaks show that coronaviruses will be a threat public health (Yang et al 2020). Mutations and natural selection, as well as recombination, will continue to be a common characteristic of coronaviruses (Yeşilbağ and Aytoğu 2020). On the other hand, high prevalence and widely geographical distribution as well as cross-species infection of the Cov and increased human-animal interaction are another risk factors for probable emerging of new Cov infections in the future (Hasöksüz et al 2020). Based on what we learned from these outbreaks, it seems important to create a roadmap for future epidemics or pandemics. Achieving a SARS-CoV-2 vaccine is a very important step in preventing the disease, but it may be ineffective to new and possible Cov strains and we should always be prepared for





the next outbreak (Yang et al 2020). It has been suggested that bats and birds are suitable reservoirs for the incubation and evolution of coronaviruses (Knipe and Howley 2013). For this reason, it is important to investigate bats and birds in proactive surveillance studies of coronaviruses, which could function as an early warning system.

Even before the COVID-19 pandemic was declared, unprecedented drug and vaccine studies had begun all over the world and are continuing at great speed. Researchers in countries across the world continue to work in great synergy. Many epidemiological studies are being conducted in human and animal populations, as well as validation studies of rapid testing methods. Failed or inconclusive vaccine studies conducted after previous outbreaks, such as SARS and MERS, should not be considered a bad precedent for COVID-19. While other diseases have been limited to a certain number of epidemics in certain countries, COVID-19 is a pandemic, and there are many more studies on it.

The rapid and early identification of the viral genome from suspected cases is crucial. In light of experiences gained from the first CoV epidemic (SARS), personal and environmental hygiene should be maintained in the health sector (Abdullah et al 2003, Cheng et al 2013). Contact follow-up, strict isolation of active patients and the quarantine of close contacts should be applied in the early period (Abdullah et al 2003). Establishing, developing and isolating triage clinics, as well as establishing pandemic hospitals and restricting visitors, are important in controlling infection and reducing human-to-human transmission (Pang et al 2003). The public should be informed and educated about individual measures to curtail the epidemic (Yang et al 2020). It is emphasized that there should be a global strategy in the struggle against COVID-19. Research, clinical efforts and increase of public awareness are suggested as three main components of this strategy (Azkur et al 2020). In addition to the rapid sharing of information, the implementation of common global measures and treatments will contribute to the control of the disease and reduce the all kind of losses (Yeşilbağ and Aytoğru 2020). In China, which experienced the SARS epidemic and has collected information about what should be done in such an epidemic, COVID-19 was taken under control in a shorter time than in other countries, and China's total number of cases and case-fatality rates are well below the world average. Marginal gains are being made in controlling the COVID-19 pandemic, but other threats to public health should not be ignored. It is suggested that child mortality may increase by 45% and maternal mortality by 39% due to, for example, quarantines, interruptions in vaccination programs, and the capacity of health institutions being under strain, as well as care and nutritional conditions in low-income countries, and the fear of going to see a medical professional for an examination, even in the case of serious illness, during and after COVID-19 (Robertson et al 2020). Similarly, research fo-

ocusing on the COVID-19 outbreak has affected preparedness efforts regarding other outbreaks. COVID-19 has augmented our knowledge of pandemic preparation, worst-case scenarios still should be considered, and pandemic pathogens other than coronaviruses should not be ignored (Naguib et al 2020).

'ONE HEALTH' approach is an opportunity to identify zoonoses that can cause pandemics before they infect human hosts. The enormous costs incurred in the COVID-19 pandemic have clearly demonstrated the need to be proactive. Moreover, COVID-19 pandemic has shown that a one health perspective with an emphasis on surveillance on wildlife and people who breed, hunt or sell these animals gives a chance in the prevention and the mitigation of these diseases (Naguib et al 2020).

### Conclusion

COVID-19 pandemic is still continuing and it has affected daily life globally as well as causing human deaths. The implementation of control measures in all countries around the world, both in terms of health expenditures and in order to prevent further increase in spread, has had a great economic impact. However, when the case and death rates are compared with the health systems, economic conditions or population densities of the countries, a great paradox can be observed. Despite the small population of other countries, the total number of cases is incomparably higher than China. Examining the case-fatality rates are in contrast with the population, health system and economic development; they are lower than 0.1% in some countries but up to 11% in some countries.

In a conclusion, while it remains uncertain when the COVID-19 pandemic will end, certain factors have had and will continue to have a substantial impact on its stabilisation and, perhaps, its end. These factors include disease awareness, good personal hygiene, sensitivity of countries and citizens in the timely implementation of control measures, quarantine, containment, disinfection, decontamination and waste management strategies, engineering controls, use of PPE's, and an increased use of developing biotechnology in virology, vaccination and drug studies. Moreover, it is thought that the gains from the COVID-19 pandemic will be beneficial in the control of future mild or serious epidemics and pandemics.

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During this study, any pharmaceutical company which has a





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